REMARKS

I. Status of the Claims

Claims 20-35 and 37-58 were canceled in an Amendment and Response to Restriction Requirement, submitted November 13, 2003. Claims 2-4 and 6-9 are canceled, and claims 1, 5, 10, 15-17, 19 and 36 are amended in the Amendment submitted herewith. Thus, claims 1, 5, 10-19 and 36 are presently pending in the application.

II. Claims Rejected Under 35 U.S.C. § 101

Claims 1-19 and 36 are rejected under 35 U.S.C. § 101, as the claimed invention is allegedly not supported by either a specific and substantial, credible asserted utility or a well established utility. Applicants respectfully traverse this rejection.

At the time the present application was filed, it was known in the art that mGluR5 forms covalent homodimers which are linked *via* cysteine disulfide bonds in the N-terminal extracellular domain (**Exhibit A**; Romano *et al.*, *J. Biol. Chem.*, 271(45):28612-28616, 1996) and that glutamate binding resides in this extracellular domain (Takahashi *et al.*, *J. Biol. Chem.*, 268(26):19341-19345, 1993). It was also known in the art that mGluR5 forms non-covalent homodimers when Cys-129 is mutated to Ser-129 and that covalent mGluR5 dimerization is not critical for mGluR5 binding or function (**Exhibit B**; Romano *et al.*, *Mol. Pharmacology*, 59(1):46-53, 2001). It has also been shown that competitive agonists and antagonists bind in the N-terminal extracellular domain of mGluR5 (**Exhibit C**; Spooren et al., Trends in Pharmacological Sciences, 22(7):331-337, 2001) and that mGluR5 forms heterodimers with mGluR1. Finally, it is well established that mGluR5 (1) stimulates phospholipase C (PLC) and phosphoinositide (PI) turnover; (2) is present in a number of key central nervous system structures including the hippocampus, cortex, thalamus and spinal cord (**Exhibit D**; Bordi and Ugolini, *Progress in Neurobiology*, 59:55-79, 1999); and (3) its role in pain/analgesia, anxiety and depression has been validated in rat and mouse models (**Exhibit C**; Spooren et al., Trends in Pharmacological Sciences, 22(7):331-337, 2001).

Applicants have identified, isolated and characterized, from a human brain derived cDNA library, a full-length open reading frame (SEQ ID NO:1) encoding a protein referred to in the specification as mGluR5M (SEQ ID NO:2). As the name implies, the mGluR5M protein is significantly similar to the N-terminus of the metabotropic glutamate receptor 5 (mGluR5), as detailed in Example 1 of the specification (page 68, line 20 through page 69, line 2). For example, the full-length human mGluR5M protein consists of 369 amino acids as set forth in SEQ ID NO:2, wherein amino acids 1-303 (FIG. 2) are 97% identical to the N-terminal amino acids of human mGluR5 extracellular binding domain (*i.e.*, 1-370 of SEQ ID NO:4). The mGluR5 protein also shares conserved cysteine (*e.g.*, Cys-57 and Cys-99), serine (Ser-152) and threonine (Thr-172) residues with mGluR5 (FIG. 2 and page 6, line 35 through page 7, line 14). Analysis of mGluR5M mRNA tissue distribution demonstrated that mGluR5M is predominantly expressed in neural tissue (Example 1, page 69, lines 5-36). Finally, Applicants data in Table 1 (page 71) demonstrates that the full-length human mGluR5M protein forms a heterodimer with full-length human mGluR5.

The specification of the present application states that in one embodiment, the mGluR5M protein of the invention is used in a cell-based assay to identify small molecules (test compounds) that modulate the dimerization of mGluR5:mGluR5M (page 46, line 3 through page 47, line 10). The specification sets forth several methodologies for assaying mGluR5:mGluR5M binding interactions and test compound modulation of the same. Thus, Applicants have asserted a "specific" utility of the present invention.

As set forth *supra*, mGluR5 agonists and antagonists bind in the mGluR5 N-terminal domain (**Exhibit D**), mGluR5 non-covalent homodimers are functionally relevant (**Exhibit A**), and the mGluR5 receptor is a therapeutically important target in the areas of pain (Walker *et al.*, *Neuropharmacology*, 40:1-9, 2001; Walker *et al.*, *Neuropharmacology*, 40:10-19, 2001), depression (Tatarczynska *et al, British J. of Pharmacology*, 132:1423-1430, 2001) and anxiety (Spooren *et al., J. of Pharm. and Exp. Therapeutics*, 295(3):1267-1275, 2000). Thus, Applicants assert that at least one "substantial" and "credible" utility of the presently claimed mGluR5M protein (and nucleic acid molecules encoding the same) is its use in

assays for identifying compounds which modulate mGluR5:mGluR5M dimer activity. Applicants therefore respectfully request withdrawal of the rejection of claims 1-19 and 36 are rejected under 35 U.S.C. § 101.

III. Claims Rejected Under 35 U.S.C. § 112, First Paragraph

Claims 1-19 and 36 are rejected under 35 U.S.C. § 112, first paragraph, as the claimed invention is allegedly not supported by either a specific and substantial, credible asserted utility or a well established utility, and as such, a person of skill in the art would not know how to use the claimed invention. Applicants respectfully traverse this rejection.

For the reasons set forth above, Applicants' contend that specification asserts at least one substantial and credible utility of the claimed invention, and as such, respectfully request withdrawal of the rejection of claims 1-19 and 36 under 35 U.S.C. § 112, first paragraph.

Claims 1-19 and 36 are rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the enablement requirement. The Action states that "Applicants claims are directed to peptides with greater than single amino acid substitutions as encompassed by % identity, to the N-terminal mGluR-like domains and to C-terminal unique domains". In order to expedite the allowance of the claims, Applicants have amended claims 1-19 and 36, deleting the phrase "at least 80% identical to the amino acid sequence". Applicants assert that claims 1-19 and 36, as amended, are enabled by the specification and respectfully request withdrawal of the enablement rejection under 35 U.S.C. § 112, first paragraph.

Claim 12 is also rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply the enablement requirement. The Action states that it is not clear that cell lines possessing the properties of ATCC deposit (Accession No. PTS-2775 [sic]) are known and publicly available, and because the claims require the use of ATCC Accession Number PTS-2775 [sic], a suitable deposit of said cell line claimed in claim 12 is required. "Without publicly available deposit of the above cell line, one of ordinary skill in the art could not be

assured of the ability to practice the invention as claimed". Applicants respectfully traverse this rejection.

Claim 12 of the present invention, is directed to "an isolated nucleic acid molecule" comprising the DNA insert of the plasmid deposited with ATCC as Accession number PTA-2775. Thus, claim 12 is not directed to, nor claims, a "cell line" as indicated in the Action. Submitted herewith is a copy of the ATCC receipt of the human mGluR5M cDNA clone (**Exhibit E**; reference name YI176; ATCC Accession No. PTA-2775), deposited on behalf of Genetics Institute (now Wyeth). The deposit was received by the ATCC December 12, 2000. Thus, Applicants assert that nucleic acid molecule set forth in claim 12 complies with the requirements of 37 C.F.R. § 1.801-1.809 and is enabled under 35 U.S.C. § 112, first paragraph. Applicants therefore respectfully request withdrawal of the rejection of claim 12.

Claims 1-11, 15-19 and 36 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement. The Action states that the language of the claims is directed to percent identity, hybridizing sequences under stringent conditions, N-terminal mGluR-like domains and C-terminal unique domains, without describing a functional significance or activity of the claimed sequences. Applicants respectfully traverse this rejection.

Claims 1, 4 and 5 have been amended in the Amendment submitted herewith, wherein the phrase "at least 80% identical to the amino acid sequence" has been deleted. Thus, Applicants assert that the amendment of claims 1, 4 and 5 obviates the written description rejection with respect to percent sequence identity.

Without acquiescing to the rejection based on the terms N-terminal mGluR-like domains and C-terminal unique domains, in order to advance claims to allowance, the phrases "N-terminal mGluR-like domain" and "C-terminal unique domain" have been deleted from pending claims 1 and 10.

Further, Applicants assert that an isolated nucleic acid molecule obtained *via* stringent hybridization to a nucleic acid molecule of SEQ ID NO 3 or 1, as set forth in claims 10 and 11, respectively, is supported by the specification and meets the written description

requirement of 35 U.S.C. § 112, first paragraph. To satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonable conclude that the inventor had possession of the claimed invention (*University of California v. Eli Lilly Co.*, 119 F.3d, 1559, (1997)). The claimed nucleic acid sequences are reduced to practice by virtue of their structural formulae (*i.e.*, SEQ ID NO:1 and SEQ ID NO:3), and as such, Applicants have demonstrated possession of the claimed subject matter. In addition, the specification, at page 16, line 3 through page 17, line 10, describes "stringent hybridization" conditions for obtaining said isolated nucleic acid molecules. Thus, Applicants assert that claims 10 and 11 are supported by the written description of the specification.

Applicants therefore respectfully request withdrawal of the rejection of claims 1-11, 15-19 and 36 are rejected under 35 U.S.C. § 112, first paragraph.

IV. Claims Rejected Under 35 U.S.C. § 102(e)

Claims 1-11, 15-19 and 36 are rejected under 35 U.S.C. § 102(e) as allegedly being anticipated by Wong *et al.*, U.S. Patent Application Publication US 2002/0142952, filed March 29, 2001 and published November 03, 2002. The Action alleges that Wong *et al.* teach an amino acid sequence and nucleic acid sequence which share high sequence identity with SEQ ID NO:2 and SEQ ID NO:1 of the present invention, respectively. Applicants respectfully traverse this rejection.

The instant application, U.S. Application No. 10/027,923, filed December 21, 2001, claims benefit of U.S. Provisional Application No. 60/257,589, filed December 22, 2000. Applicants assert that the Wong *et al.* application (U.S. Application No. 09/822830, now abandoned), and the instant application, share a common inventor, Kamalakar Gulukota. Submitted herewith is a 37 C.F.R. § 1.132 declaration of Dr. Gulukota (**Exhibit F**), stating that the subject matter of SEQ ID NO:61, disclosed in the Wong *et al.* U.S. Application No. 09/822830, was not invented "by another", and therefore not anticipated under 35 U.S.C. §

102(e). Applicants therefore respectfully request withdrawal of the rejection of claims 1-11, 15-19 and 36 are rejected under 35 U.S.C. § 102(e).

If there are any matters which may be resolved or clarified through a telephone interview, the Examiner is requested to contact the undersigned Agent at the number indicated.

The notice set a three-month period to comply, to and including May 10, 2004. Thus, this response is believed to be timely filed. Should any fees be deemed necessary, the Commissioner is authorized to deduct said fees from Deposit Account No. 01-1425.

Respectfully submitted,

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